

REMARKS

I. Status of Claims

Claims 1-27 were previously cancelled, and claims 63 and 67 are currently cancelled. Claims 28-59, 73, 74, and 79-98 have been withdrawn from examination at this time. Claims 60-61, 64-66, 68-71, and 77 are currently amended. Claims 99-100 are newly added. Therefore, claims 70 and 71, and the linking claims 60-61, 64-66, 68-69, 72 and 75-79, and claims 99-100 are under examination (*i.e.*, claims 60-62, 64-66, 68-72, 75-79, and 99-100).

Support for the amendments to the claims can be found throughout the specification as originally filed. For example, support for the amendment to claim 60 can be found in original claim 63 and 67. Claims 61, 64-66, 68, and 69 were amended to provide proper antecedent basis. The amendments to claims 65-66 and 68-71, reciting the numbering scheme are supported in the specification as originally filed, such as at page 7, lines 15-28; page 10 line 3 to page 11, line 20; Examples 1, 4, 5, and 6; and Figures 1 and 2.

Support for new claims 99 and 100 can be found in claim 69 as originally filed and in the specification at page 4, lines 15-18.

II. Amendments to the Specification

The paragraph beginning at page 1, line 1 is amended to correct typographical errors.

The paragraph beginning at page 8, line 24 is amended to reflect that Figures 9A and 9B are described. The paragraph beginning at page 8, line 30 is amended to reflect that Figures 10A and 10B are described.

The paragraph beginning at page 10, line 24 is amended to correct an inconsistency in the terminology for “catalytic domain.”

The paragraph beginning at page 12, line is amended to clarify that the term “FACScan” is a trademark.

The paragraph beginning at page 23, line 3 is amended to indicate that mutanolysin is a generic term. It should be noted that the underlining in the Laemmli citation is found in the original application and does not indicate that the citation was added at this time. The paragraph

beginning at page 23, line 17 is amended to clarify that the term “Ficoll” is a registered trademark and that the term “Hypaque” is a trademark. It should be noted that the Booth citation contains an underline in the original specification and does not indicate that the citation was added at this time.

The paragraph at page 32, line 14 is amended to correct the address of the American Type Culture Collection.

The paragraph beginning at page 32, line 26 is amended to clarify that that term “Sepharose” is a registered trademark. It should be noted that the underlining in the nucleic acid sequence is found in the original application and does not indicate that the six nucleotides are added at this time.

The paragraph beginning at page 34, line 3 is amended to clarify that the term “Eppendorf” is a registered trademark. It should be noted that the underlining in the O’Connor *et al.* citation is found in the original application and does not indicate that the citation was added at this time.

The paragraph beginning at page 42, line 20 is amended to clarify that the terms “Sequenase” and “Qiaquick” are trademarks, and that the term “Stratagene” is a registered trademark.

The paragraph beginning at page 44, line 4, and the paragraph beginning at page 45, line 24 are amended to clarify that the term “Invitrogen” is a trademark.

The paragraph beginning at page 45, line 24 is amended to clarify that the term “Invitrogen” is a trademark.

III. Non-Statutory Double Patenting Rejections

Claims 60-63, 67, 68, 77 and 78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 22 and 28 of U.S. Patent No. 6,270,775. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned

with this application. A terminal disclaimer is enclosed herewith, thereby overcoming this rejection.

Claims 60, 61, 77 and 78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 22 and 28 of U.S. Patent No. 5,846,547. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. A terminal disclaimer is enclosed herewith, thereby overcoming this rejection.

Applicants request that the obviousness-type double patenting rejections be withdrawn.

IV. Rejections under 35 U.S.C. Section 112

A. First Paragraph - Enablement

The examiner has indicated that claims 69-72 are rejected under 35 U.S.C. Section 112, first paragraph, because the specification while being enabling for the enzymatically inactive SCP variants having the specific amino acid substitutions, *i.e.*, SCPA49D130A, SCPA49H193A, SCPA49N295A, SCPA49S512A, SCPA1D130A, SCPA1H193A, SCPA1N295A, SCPA1S512A, SCPBD130A, SCPBH193A, SCPBN295A, and SCPBS512A, does not reasonably provide enablement for the large number of enzymatically inactive SCP variant members or species currently encompassed within the scope of the instant claims, having one or more conserved or non-conserved amino acid modifications or substitutions at positions 260, 261, 262, 415, 416, 417, 130, 193, 295 or 512, as claimed in a broad sense.

First, it is unclear to the Applicant whether the examiner has examined claims 73 and 74, which specifically recite SCPA49D130A, SCPA49H193A, SCPA49N295A, SCPA49S512A, SCPA1D130A, SCPA1H193A, SCPA1N295A, SCPA1S512A, SCPBD130A, SCPBH193A, SCPBN295A, and SCPBS512A, or whether claims 73 and 74 stand withdrawn. It appears from the examiner's comments on pages 5-8 of the Office Action dated 3/9/04 that these claims have been examined. Applicants request clarification of this point.

The examiner indicated at page 6 of the Office Action that the claimed product is a peptide of unlimited size or length. The claims have been amended to recite that the SCP comprises the catalytic domain of SCP, thereby providing adequate structural description of the peptide.

The examiner indicated at page 6 of the Office Action that there is no evidentiary support that an SCP variant with more than one amino acid substitution, if constructed, would be enzymatically inactive and immunogenically functional as a vaccine specifically against streptococci. Applicants have made SCP double mutants in addition to the single mutants listed above. Olmsted Declaration at paragraph 2, and attached manuscript. Applicants have made double mutants from SCP from both group A and group B streptococci. These SCP double mutants contained a D130A/S512A substitution, and were found to be enzymatically inactive and immunogenically functional as vaccines specifically against streptococci. Therefore, claims 69-72 are enabled by the recitation of "one or more" amino acids.

Claims 99 and 100 have been newly added. Insofar as the present rejection is applied to these claims, it is hereby traversed. These claims recite an enzymatically inactive SCP that contains the catalytic domain of SCP, having a substitution at one or more (or one or two) of amino acid residues 130, 193, 295 or 512. In these claims, the substitution is where the native amino acid residue has been replaced with an alanine, valine, leucine, isoleucine, proline, phenylalanine, tryptophan or methionine residue. These amino acid residues are the essential amino acids that have non-polar side chains (specification at page 4, lines 13-21). It is well-known in the art that such substitutions are generally made without affecting the over-all conformation of a protein. Once Applicants made the discovery that SCP is a protein that can generate an effective immune response in an organism, and that these specific amino acid residues were important in enzymatic activity, as taught by the specification, it would have been within the skill of an artisan to generate the peptides recited in the claims, and would have had a reasonable expectation of success.

Applicants request that the 35 U.S.C. Section 112, first paragraph rejection be withdrawn.

B. Second Paragraph

The examiner rejected claims 60-72 and 75-78 under 35 U.S.C. Section 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter.

- (a) Claims 60-65, 67, 68, 70, 71 and 75-78 were held vague and confusing in the use of the "SCP" abbreviation in the claims. The base claim, claim 60, has been amended to recite the full terminology "Streptococcal C5a peptidase (SCP)."
- (b) Claim 61 was held to have improper antecedence in the limitation "of claim 60 wherein the vaccine." Claim 61 has been amended to recite "of claim 60 wherein the peptide."
- (c) Claim 61 was held to be vague and indefinite in the recitation of the term "variant." Claim 61 has been amended to delete this term. Insofar as this rejection is applied to claim 77, claim 77 has been similarly amended.
- (d) Claims 65 and 66 were held to have improper antecedence in the limitation "of claim 64 wherein the DNA" because claim 64 does not recite any DNA. Claims 65 and 66 have been amended to delete any reference to DNA.
- (e) Claim 65 was held to be vague and indefinite in the recitation "DNA encodes and SCP." Claim 65 has been amended to delete any reference to DNA.
- (f) Claims 65, 66, 68 and 69 were held to be confusing because the claims are to a peptide, yet the claims include the recitation to DNA. Claims 65, 66, 68 and 69 have been amended to delete any reference to DNA.
- (g) Claims 65, 66 and 68-72 were held to be vague and indefinite in the recitation of one or more amino acid residues, such as 260, 262, 262, 415, 130, 512 etc. without identifying the claimed peptide by its SEQ ID number. The examiner requested clarification that the numbering starts after the signal sequence or before the signal sequence and in a full length polypeptide or truncated peptide. The claims have been amended to recite that the amino acid numbering of the peptide is consistent with the numbering of a full-length SCP that includes a signal sequence. Support for this amendment can be found in the specification as originally filed, such as at page 7, lines 15-28; page 10, line 3 to page 11, line 20; Examples 1, 4, 5, and 6;

and Figures 1 and 2. This numbering scheme is consistent with the published literature. (See, e.g., Anderson *et al.*, *Eur. J. Biochem.* 269:4839-4851 (2002); Cheng *et al.*, *Infect. and Immun.* 70:2408-2413 (2002) (copies enclosed herewith)).

(h) Claim 60 was held to be vague and indefinite in reciting the phrase “peptide comprising . . . SCP.” The term “comprising” has been deleted from the claim.

Applicants assert that these rejections are rendered moot in view of the amendments to the claims. Therefore, Applicants respectfully request that these rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

V. Rejections under 35 U.S.C. Section 102

A. Rejection under 35 U.S.C. Section 102(f)

The examiner rejected claims 60, 77 and 78 under 35 U.S.C. Section 102(f), stating that the Applicants did not invent the claimed subject matter. The examiner cites to U.S. Patent No. 5,846,547 (“the ‘547 patent), which names Cleary as the sole inventor, whereas the present application names Cleary and Stafslieen as co-inventors. Therefore, the examiner concludes that the instant inventors did not invent the subject matter sought to be patented in the instant application.

It should be noted that the instant application is a continuation-in-part of U.S. Application Serial No. 08/589,756 that matured into the ‘547 patent. Because the scope of the instant application is broader than that of the parent application, the inventorship of the two applications is different. It is well known that a named inventor on a patent application need not be an inventor of all of the claims included in the patent application. Further, the instant application claims priority to U.S. Application Serial No. 08/589,756. Thus, the patent that issued from U.S. Application Serial No. 08/589,756 is not citable as prior art against the instant application.

Therefore, Applicants respectfully request that this rejection under 35 U.S.C. § 102(f) be withdrawn.

B. Rejection under 35 U.S.C. Section 102(b)

The examiner rejected claim 60 under 35 U.S.C. Section 102(b), as being anticipated by Cleary *et al.*, U.S. Patent No. 4,772,584 (“the ‘584 patent”). Claim 60 has been amended to recite the features of originally-filed claim 67.

The ‘584 patent is directed to the purification of an enzymatically active streptococcal chemotactic factor inactivator polypeptide (“SCFI”) from virulent strains of group A streptococci. SCFI of the ‘584 patent was later renamed Streptococcal C5a peptidase (SCP). In the experiments described in the ‘584 patent, the inventors tried extracting SCFI by means of a trypsin and detergent extraction procedure, which resulted in peptide bond cleavage of some of the extracted proteins rendering them enzymatically inactive. See, the ‘584 patent at col. 8, lines 3-23. Since the only way that the SCFI proteins were being rendered enzymatically inactive was by peptide cleavage of the protein, the enzymatically inactive proteins would necessarily not comprise the full catalytic domain, otherwise they would have been enzymatically active. The only proteins present would have been enzymatically active proteins, which may or may not have contained the full catalytic domain, or enzymatically inactive proteins, which would not have contained the full catalytic domain. There is no teaching or suggestion in the ‘584 patent of an isolated and purified peptide comprising an enzymatically inactive Streptococcal C5a peptidase (SCP) peptide, wherein the peptide comprises the catalytic domain of SCP, as recited by the present claims.

Therefore, Applicants respectfully request that this rejection under 35 U.S.C. § 102(b) be withdrawn.

C. Rejection under 35 U.S.C. Section 102(e)

The examiner rejected claim 60-62 and 75-78 under 35 U.S.C. Section 102(e), as being anticipated by Green *et al.*, U.S. Patent No. 6,100,380 (“the ‘380 patent”). Claim 60 has been amended to recite the features of originally-filed claim 67. Claims 61-62 and 75-78 all depend directly or indirectly from claim 60.

The '380 patent discloses an isolated Gly-Lys dipeptide. It does not, however, teach or suggest an isolated and purified peptide comprising an enzymatically inactive Streptococcal C5a peptidase (SCP) peptide, wherein the peptide comprises the catalytic domain of SCP, as recited by the present claims. Thus, the '380 patent does not anticipate the present claims.

Therefore, Applicants respectfully request that this rejection under 35 U.S.C. § 102(e) be withdrawn.

D. Rejection under 35 U.S.C. Section 102(b)

The examiner rejected claim 60-69 under 35 U.S.C. Section 102(b), as being anticipated by Wexler *et al.*, *PNAS* 82:8144-8148 (1985). Claim 60 has been amended to recite the features of originally-filed claim 67. Claims 61-69 depend directly or indirectly from claim 60.

The Wexler *et al.* paper discloses the mechanism of action of streptococcal chemotactic factor inactivator polypeptide (SCFI), which is also called SCP. The examiner indicates that the paper teaches an SCFI enzyme where the enzymatic activity has been neutralized or terminated using SCFI-specific antiserum (abstract; page 8144, right column; and page 814 [*sic*], left column). The abstract does not make such a teaching, and there is no page 814 in this paper. The paragraph titled "Isolation of SCFI" on page 8144, right column indicates that the authors were able to isolate antiserum to SCFI, and that the specificity of the antibody was determined by neutralization of SCFI activity. The focus of these experiments in the Wexler *et al.* paper were to determine the specificity of the antibody to SCFI; therefore, only SCFI that was bound to antibody was tested to see if it still retained enzymatic activity. They did not test purified SCFI (*i.e.*, SCFI that was not bound to antibody). No where in this paper do the authors teach a purified enzymatically inactive SCFI (or SCP), as recited by the present claims. Thus, the Wexler *et al.* paper does not anticipate the present claims.

Therefore, Applicants respectfully request that this rejection under 35 U.S.C. § 102(b) be withdrawn.

Applicant : Paul Patrick Cleary et al.
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Page : 27 of 27

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CONCLUSION

Applicants respectfully submit that pending claims 60-72 and 75-79 are in condition for allowance, which action is requested. The Examiner is invited to telephone the undersigned if such would further prosecution.

Enclosed is a check in the amount of \$1,350 (\$950 for the Petition for a Three-Month Extension of Time fee, \$180 for the Information Disclosure Statement, and \$220 for the Terminal Disclaimer fee). Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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